Citation:

Appleby P, Roddam A, Allen N, Key T. Comparative fracture risk in vegetarians and nonvegetarians in EPIC-Oxford. *Eur J Clin Nutr.* 2007 Dec;61(12):1400-6.

PubMed ID: 17299475

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the association of fracture risk with diet group characterized as meat eater, fish eater, vegetarian or vegan in the EPIC-Oxford cohort.

Inclusion Criteria:

- Men and women aged 20 - 89 years
- Postal method targeted at vegetarians living throughout the United Kingdom
- General practice surgeries in Oxfordshire, Buckinghamshire and Greater Manchester

Exclusion Criteria:

- Participants who did not answer the question about fractures (n = 240)
- Participants who reported any type of fracture before recruitment or a fracture of the digits or ribs (n = 1,360)
- Participants whose nutrient intake data were considered to be unreliable (n = 660)

Description of Study Protocol:

Recruitment

Participants in the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Oxford) were recruited by postal methods and through general practice surgeries.

Design: Prospective Cohort Study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis

- Fracture incidence in relation to diet group was examined using Cox regression
- Analyses were stratified and adjusted for the following factors: age at recruitment, smoking, alcohol consumption, BMI, walking, cycling, other exercise or sport, amount of vigorous exercise, physical activity at work, marital status, and for women, number of children and use of hormone replacement therapy
- Relative risks and 95% confidence intervals were calculated with meat eaters as the reference category
- Further adjustments made for energy and calcium intake

Data Collection Summary:

Timing of Measurements

- Between 1993 and 2000, all participants completed a lifestyle and food frequency questionnaire, including questions relating to height and weight, smoking habits, alcohol drinking, physical activity at work and during leisure time, and marital status. Women were also asked about their reproductive history and use of hormone replacement therapy.
- Participants sent a follow-up questionnaire 5 years later

Dependent Variables

- Fracture risk based on self-report after 5 years
- Questionnaire asked whether they had suffered any fractured bones over the previous 6 years and to report the month and year of each fracture, the bones affected and the cause, categorized as a fall, road traffic accident, other accident, fracture found only by x-ray or other causes
- Incident fracture was defined as one occurring after the date of recruitment and involving bones other than the digits or ribs

Independent Variables

- Meat eaters (n = 19,249)
- Fish eaters (n = 4,901)
- Vegetarians (n = 9,420)
- Vegans (1,126)
- Energy and calcium intake estimated through food frequency questionnaire

Control Variables

- Age at recruitment
- Smoking
- Alcohol consumption
- BMI
- Walking
- Cycling
- Other exercise or sport
- Amount of vigorous exercise
- Physical activity at work
- Marital status
- For women, number of children and use of hormone replacement therapy

- Further adjustments made for energy and calcium intake

Description of Actual Data Sample:

Initial N: Recruitment questionnaire completed by 57,450 participants. Follow-up questionnaires were available for 36,956 participants.

Attrition (final N): After application of exclusion criteria, 34,696 remained in the analysis. 7,947 men and 26,749 women.

Age: aged 20 - 89 years at baseline, mean age at recruitment was 46.6 years overall

Ethnicity: not mentioned

Other relevant demographics:

Anthropometrics

Location: Oxford, United Kingdom

Summary of Results:

Numbers of incident fractures and incidence rate ratios (95% CI) by diet group, showing the effects of progressive adjustment for age, non-dietary factors and intakes of energy and calcium

Variables	Age Alone	Age and Non-Dietary Factors	Age, Non-Dietary Factors, Energy and Calcium Intake
Men and Women	P = 0.010	P = 0.23	P = 0.77
Meat eater (n = 1,092)	1.00	1.00	1.00
Fish eater (n = 261)	1.05 (0.91 - 1.20)	1.01 (0.88 - 1.17)	1.01 (0.88 - 1.17)
Vegetarian (n = 471)	1.01 (0.89 - 1.13)	1.00 (0.89 - 1.13)	1.00 (0.89 - 1.13)
Vegan (n = 74)	1.37 (1.07 - 1.74)	1.30 (1.02 - 1.66)	1.15 (0.89 - 1.49)

Other Findings

Meat eaters had the highest BMI and tended to be the least active group, while vegans had the lowest BMI and reported the highest levels of walking, cycling and vigorous exercise.

Mean energy intake was highest in the meat eaters and lowest in the vegans.

Mean calcium intakes were similar for meat eaters, fish eaters and vegetarians but were considerably lower for vegans.

In more than 182,000 person-years of follow-up,an average of 5.2 years follow-up, 343 men (4.3%)and 1,555 women (5.8%) reported one or more fractures.

Compared with meat eaters, fracture incidence rate ratios in men and women combined adjusted for sex, age and non-dietary factors were 1.01 (95% confidence interval: 0.88 - 1.17) for fish eaters, 1.00 (95% confidence interval: 0.89 - 1.13) for vegetarians, and 1.30 (95% confidence

interval: 1.02 - 1.66) for vegans.

After further adjustment for dietary energy and calcium intake, the incidence rate ratio among vegans compared with meat eaters was 1.15 (95% confidence interval: 0.89 - 1.49).

Among subjects consuming at least 525 mg/day calcium, the corresponding incidence rate ratios were 1.05 (95% confidence interval: 0.90 - 1.21) for fish eaters, 1.02 (95% confidence interval: 0.90 - 1.15) for vegetarians and 1.00 (95% confidence interval: 0.69 - 1.44) for vegans.

Author Conclusion:

In conclusion, fracture risk was similar for meat eaters, fish eaters and vegetarians in this study. The higher fracture risk among vegans appeared to be a consequence of their considerably lower mean calcium intake. Vegans, who do not consume dairy products, a major source of calcium in most diets, should ensure that they obtain adequate calcium from suitable sources such as almonds, sesame seeds, tahini, calcium-set tofu, calcium-fortified drinks and low-oxalate leafy green vegetables such as kale.

Reviewer Comments:

Vegetarians specifically targeted. All data based on self-report. Dietary assessment measured only at baseline. Incident fracture was defined as involving bones other than the digits or ribs.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes

1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	No
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A

5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	No
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	No
7.5.	Was the measurement of effect at an appropriate level of precision?	???

7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes